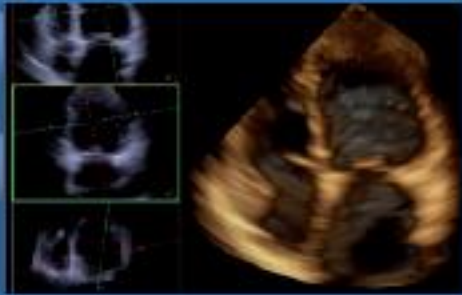


Surgical indications in ascending aorta aneurysms: What do we know?



EuroValve

January 26-27, 2017

Crowne Plaza **Barcelona**, SPAIN
www.eurovalvecongress.com

Jean-Luc MONIN, MD, PhD.

Institut Mutualiste Montsouris, Paris, FRANCE



www.imm.fr

Disclosures related to this talk :

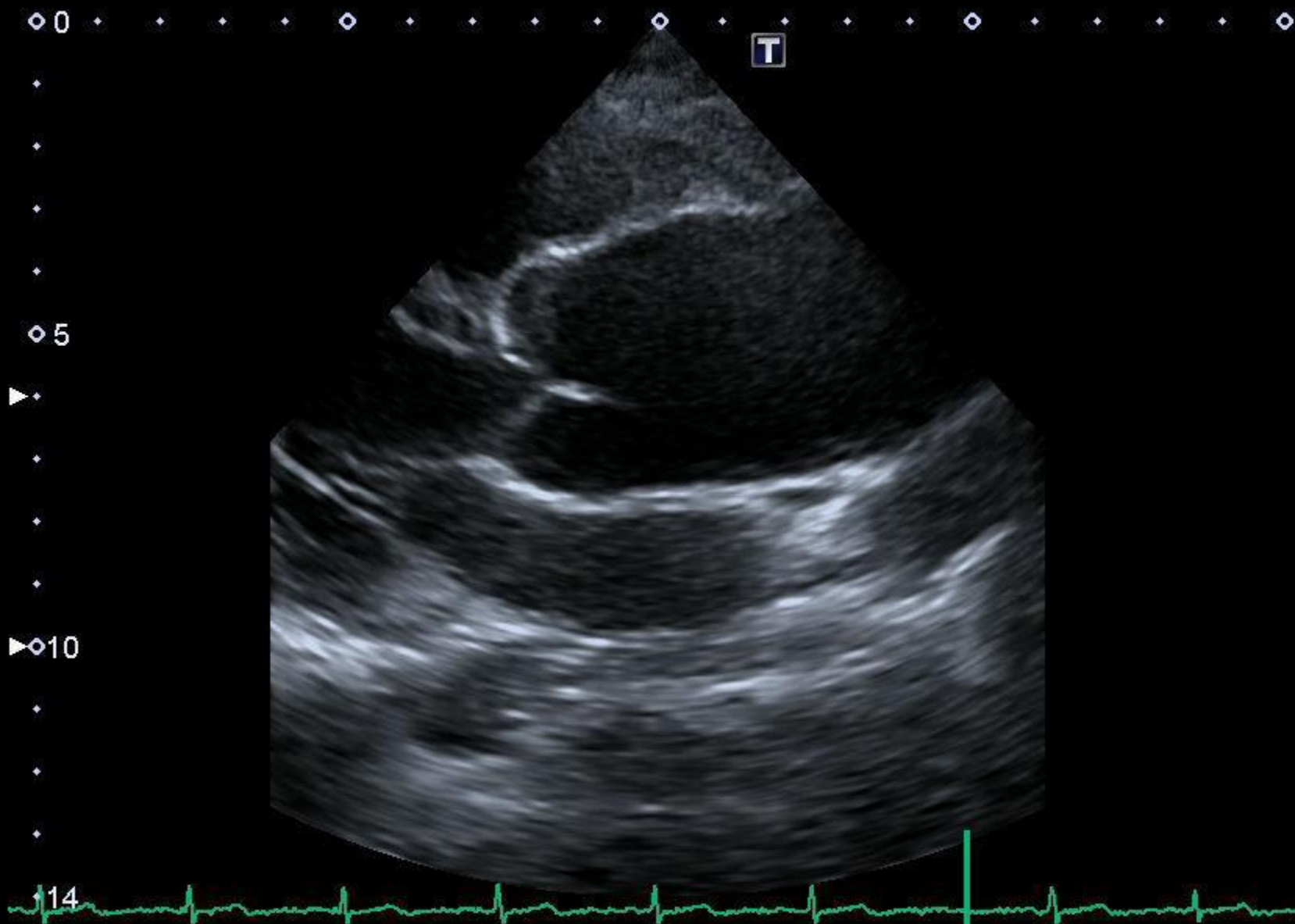
NONE



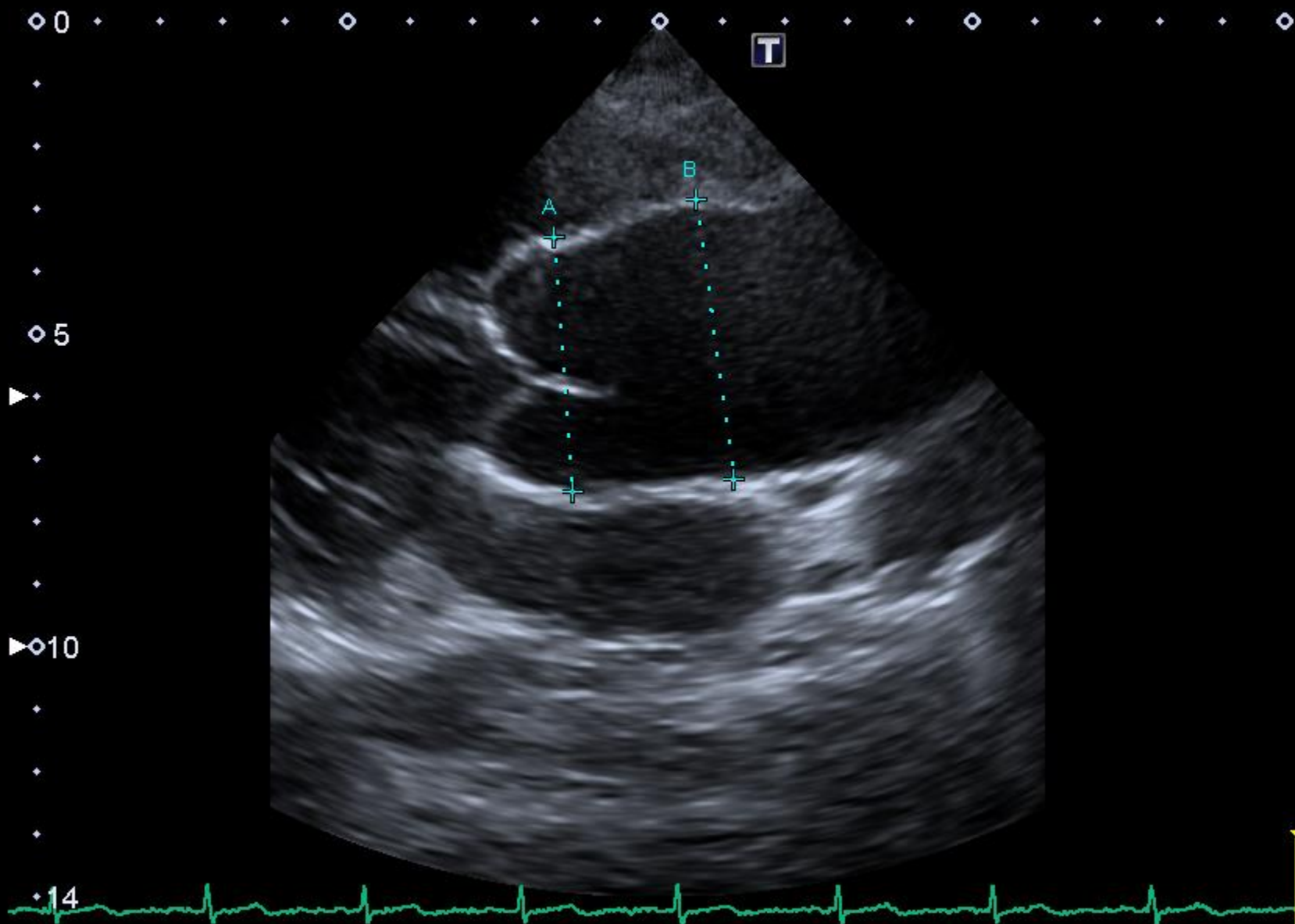
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Clinical case

- A 40 year-old woman
- Height: 172 cm/ Weight: 70 kg
- Ascending aortic aneurysm
- She wants to become pregnant (3-year old kid)
- No Marfan syndrome or bicuspid AV
- Younger sister: sudden unexplained death (at 18 years old)
- 2012 (MRI): Valsalva: 42 mm, tubular: 43 mm
- 2013 (MRI): Valsalva: 40 mm, tubular: 45 mm



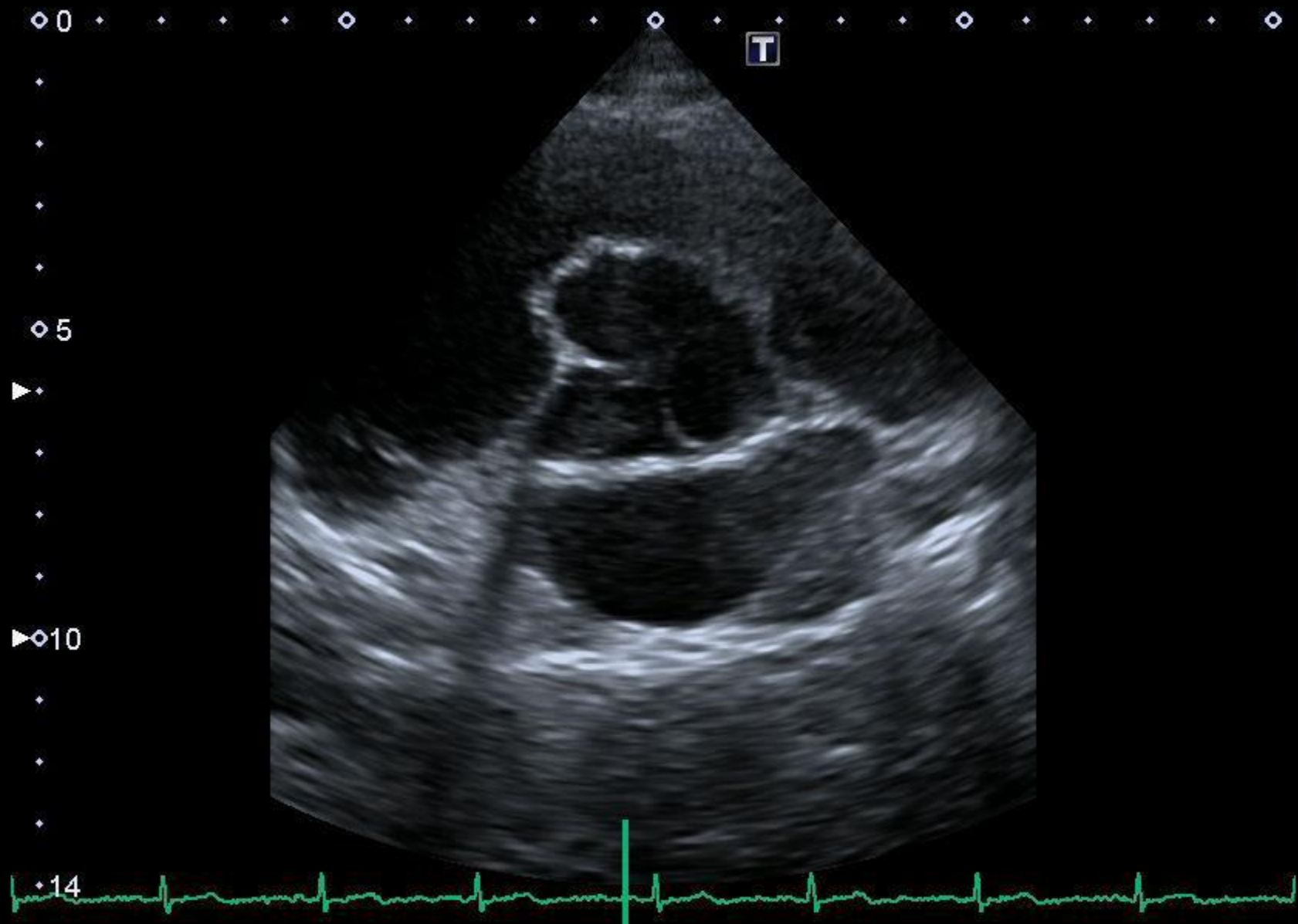
M
1.4
5S2
T2.4
46 fps
Qscan
G:86
DR:70



5S2
T2.4
46 fps
Qscan
G:86
DR:70

Dist A 40.9 mm

Dist B 45.2 mm



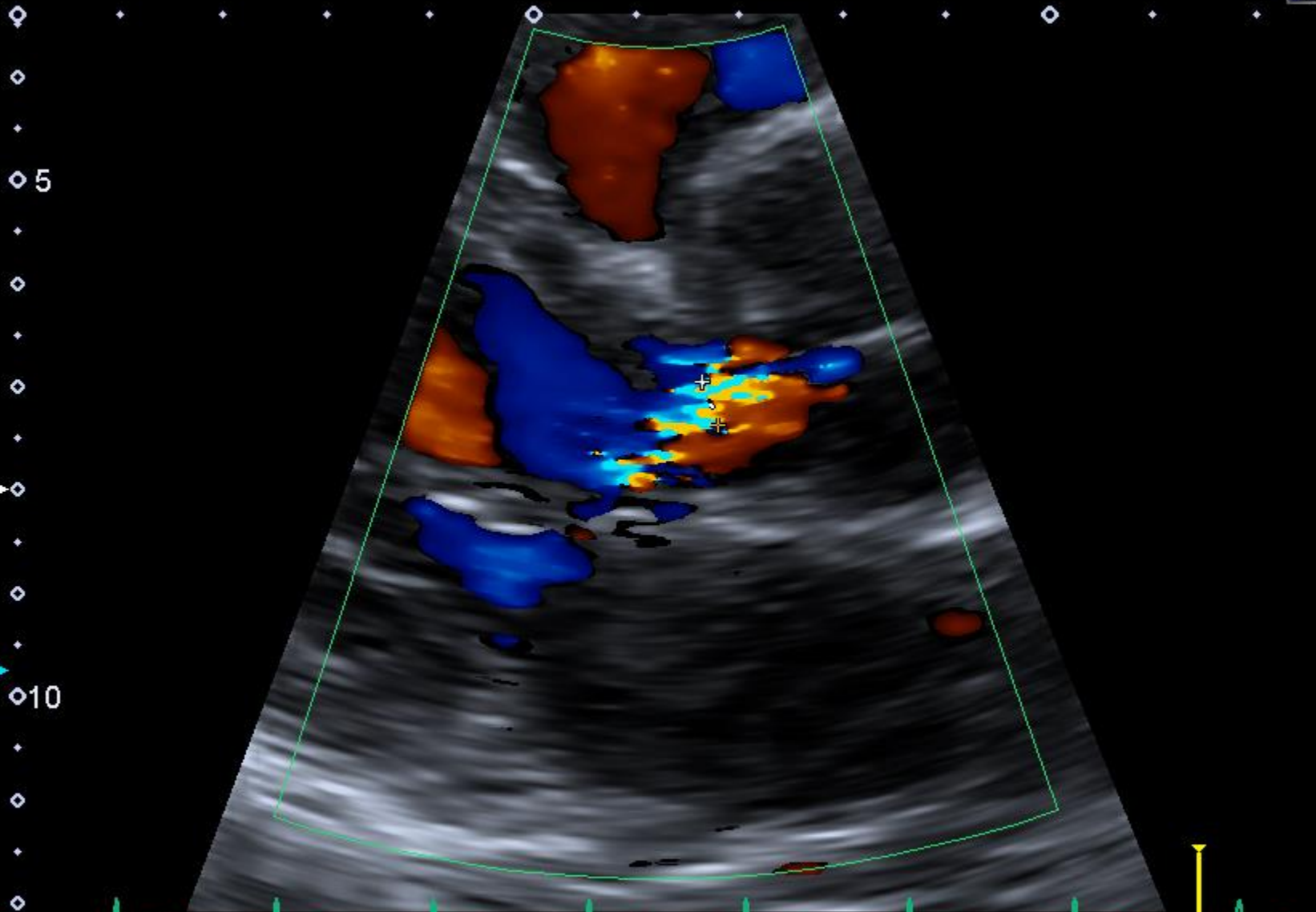
M
1.4
5S2
T2.4
46 fps
Qscan
G:86
DR:70



69.2



69.2
cm/s



5

10

5S2

T2.4

29 fps

Qscan

G:86

DR:70

CF 2.2

CG:33

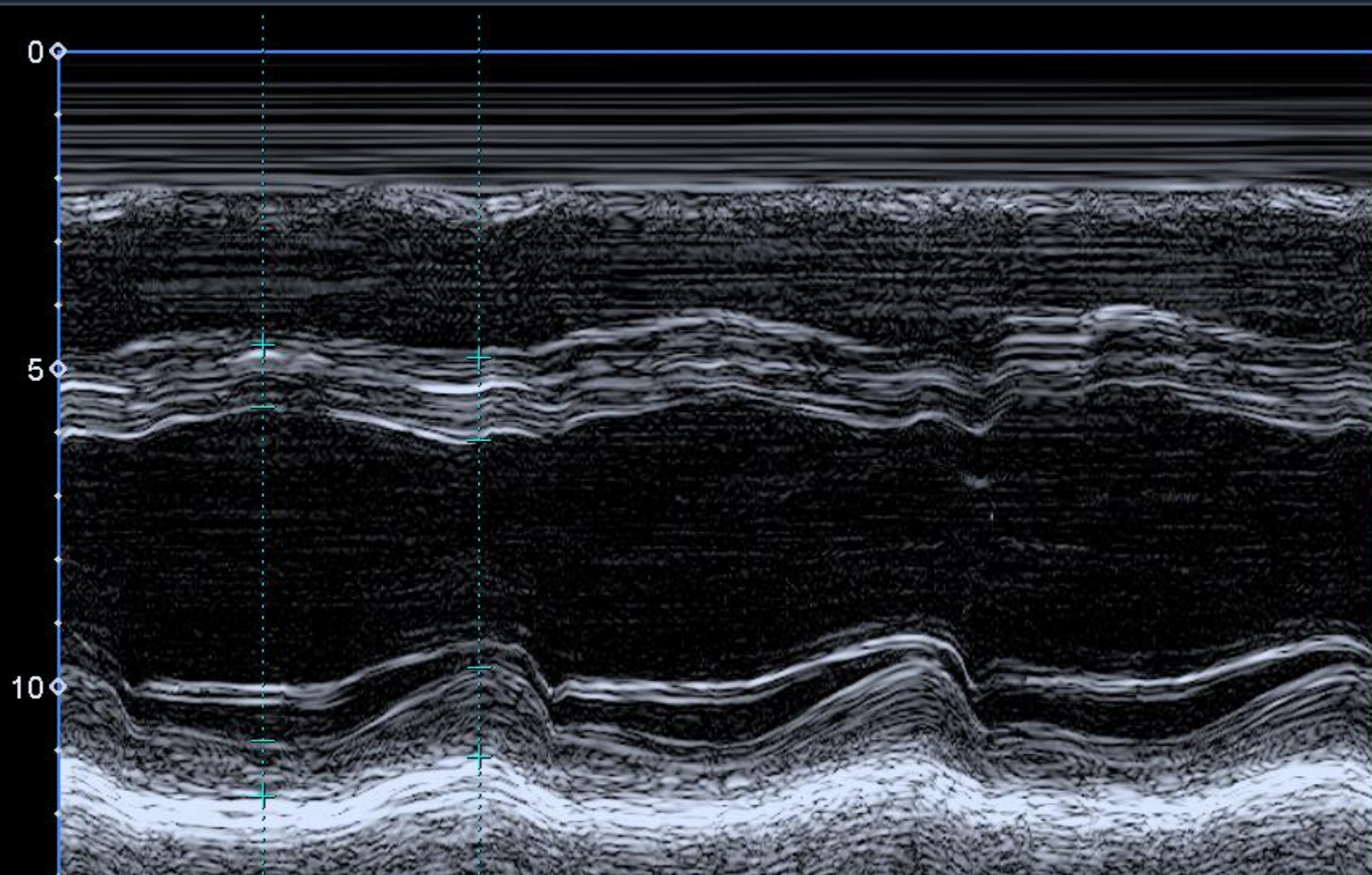
4.0k

F:2

Dist A

4.5 mm





LV Teichholz					
IVSTd	9.7 mm	LVIDd	52.5 mm	LVPWTd	8.7 mm
IVSTs	13.0 mm	LVIDs	35.7 mm	LVPWTs	14.0 mm
EDV	132.4 ml	ESV	53.3 ml	SV	79.1 ml
EF	59.7 %	FS	32.0 %	LV MASSd	220 g
				FC	79 bpm
				CO	6.249 l/min

69.2



69.2
cm/s

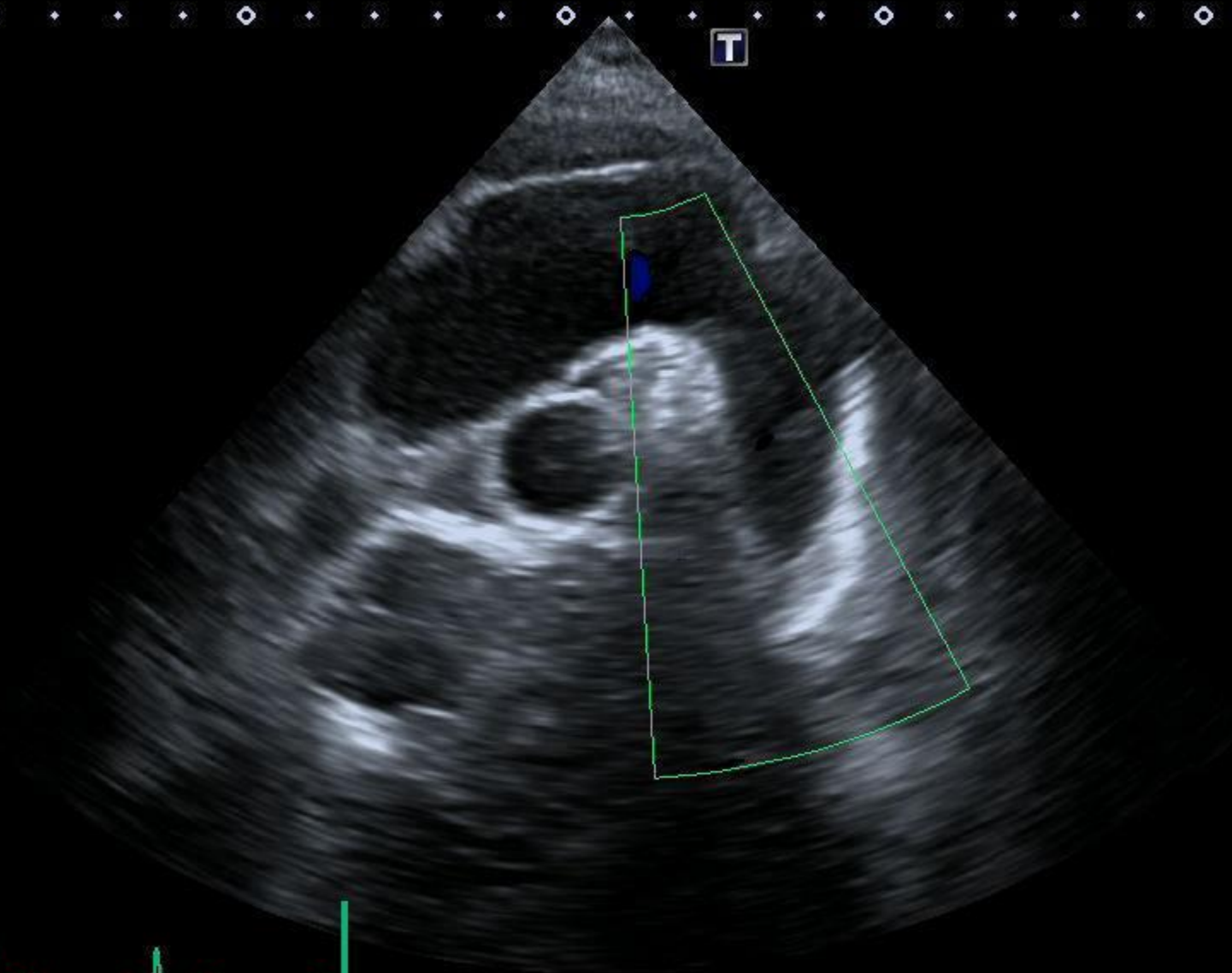
0

T

5

10

15



M
1.2
5S2
T2.4
31 fps
Qscan
G:91
DR:70
CF 2.2
CG:33
4.0k
F:2





What would we advise to this woman ?

- A. Pregnancy is temporarily contra indicated, MRI or cardiac CT is needed
- B. No contra indication for pregnancy, TTE or MRI at 1 year



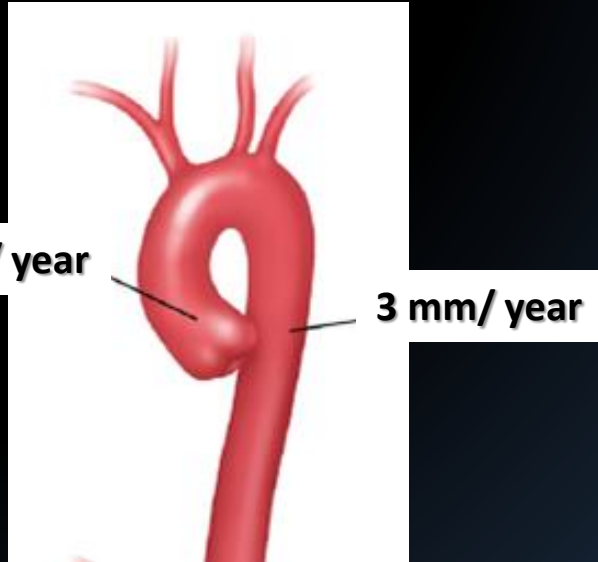
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Thoracic aortic aneurysm

Size matters

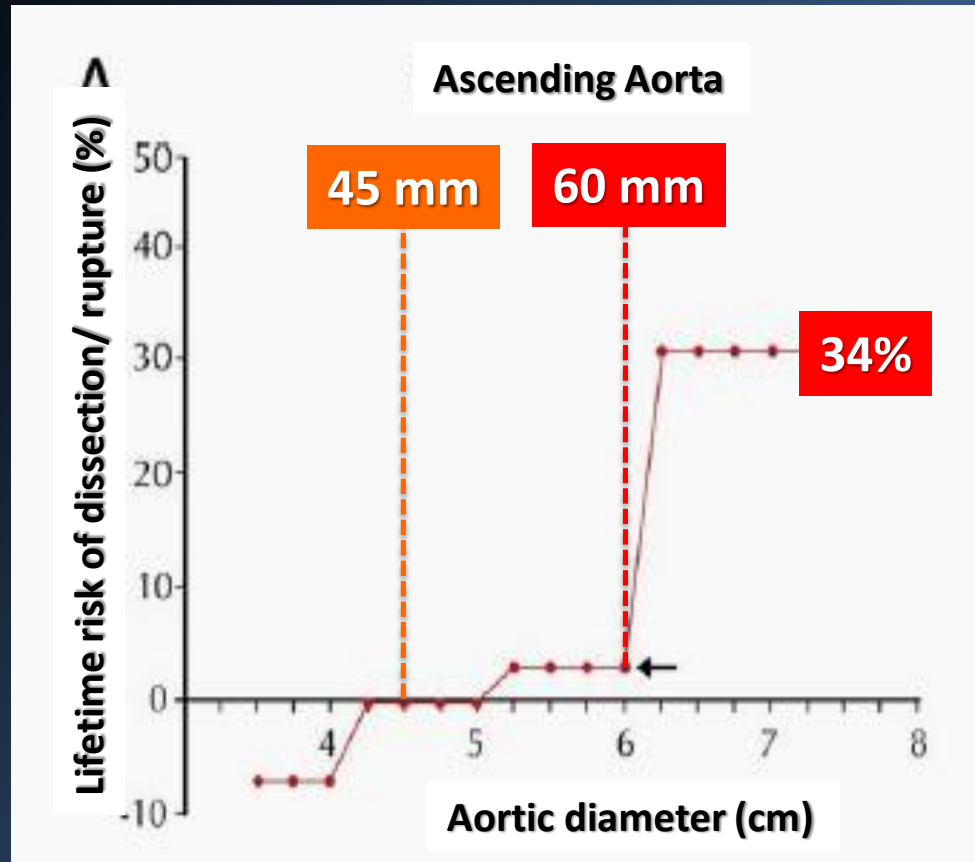


Thoracic Aortic Aneurysm: An indolent but virulent process



Rate of aortic dilatation is
EXPONENTIAL

- Expansion rate \approx 2.1 mm/ year for an initial diameter of 35-40 mm
- Expansion rate \approx 5.6 mm/ year for aneurysms \geq 60 mm

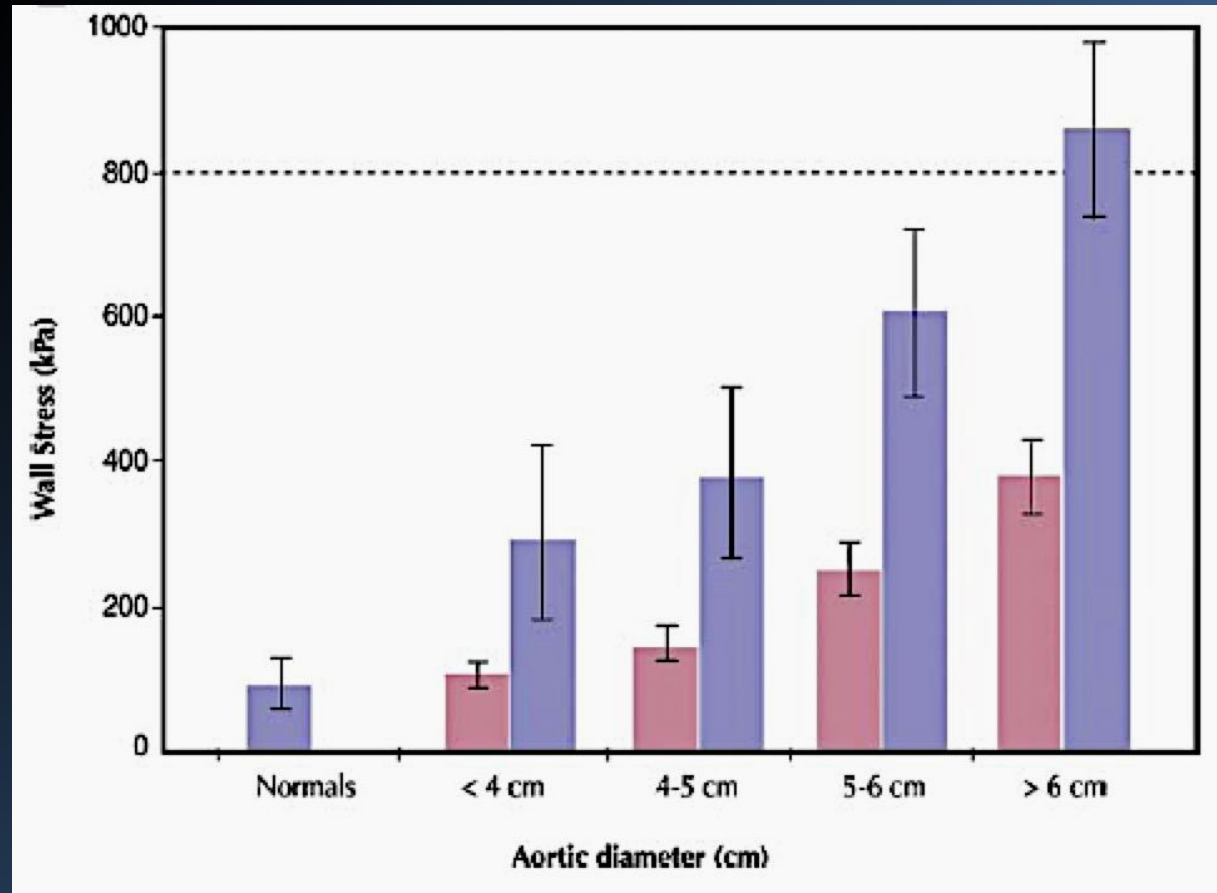




Mechanical properties of human ascending aorta : >6 cm is the limit

Exponential relationship between wall stress and aneurysm size in ascending aortic aneurysms.

- Pink columns : SBP = 100 mm Hg
- Purple columns : SBP = 200 mm Hg
- Range of maximum tensile strength of the human aorta : 800 to 1,000 kPa



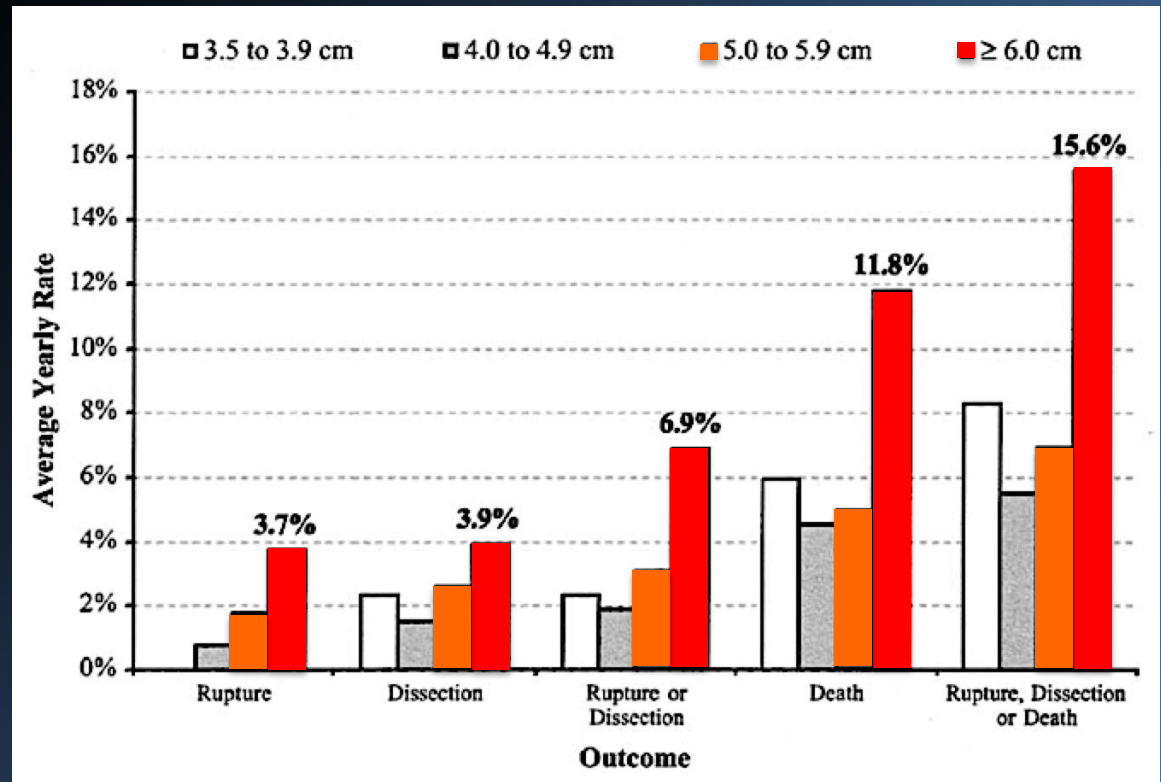


Yearly Rupture or Dissection Rates for TAA: Simple Prediction Based on Size

Retrospective analysis of 304 patients, followed up serially with thoracic aortic aneurysms at **Yale Center for Thoracic Aortic Disease**

Baseline characteristics:

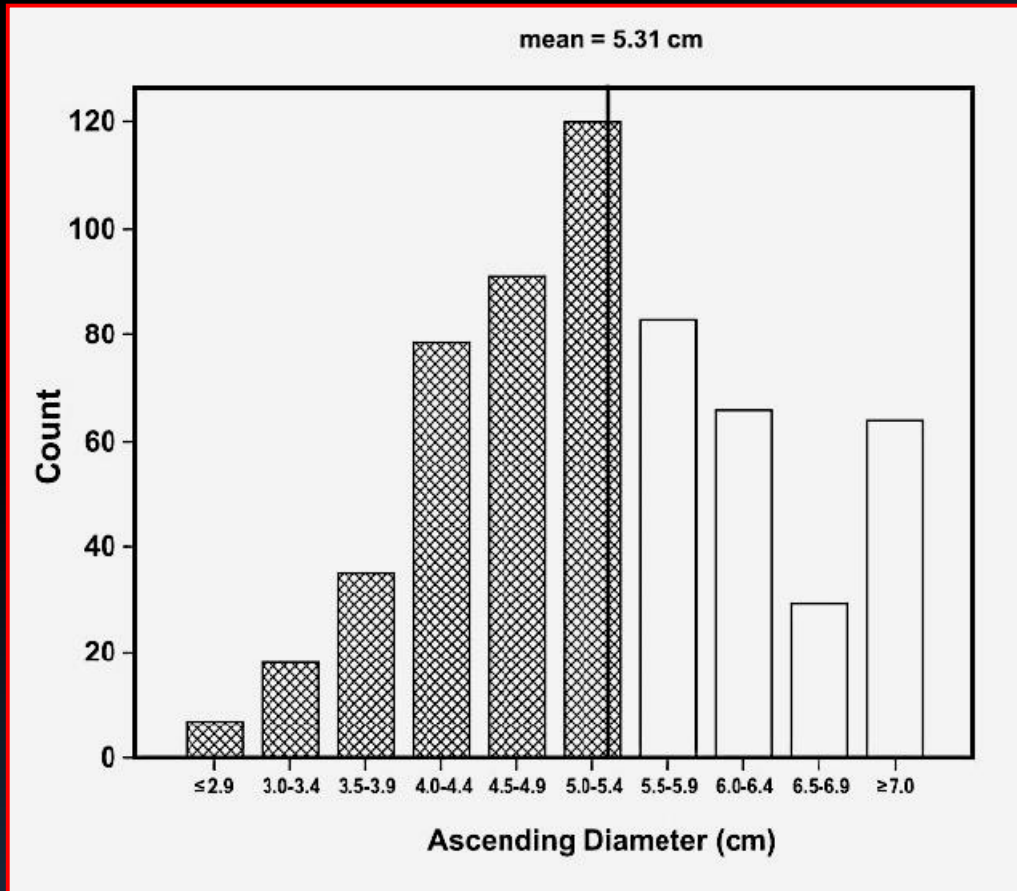
- Age: 66 years (9-94)
- Male gender: 60%
- Ascending aorta: 72%
- Marfan syndrome: 9%
- Coarctation excluded





Aortic diameter > 55 mm is NOT A good predictor of Type-A aortic dissection

Type-A dissection in 591 patients from IRAD (1996-2005, mean age: 61 years)



Ascending aorta diameter was:

- <55 mm in 349 patients (59%)
- <50 mm in 229 Pts (40%)
- The group with larger diameters (>55 mm) included more patients with Marfan or Bicuspid valves (?)

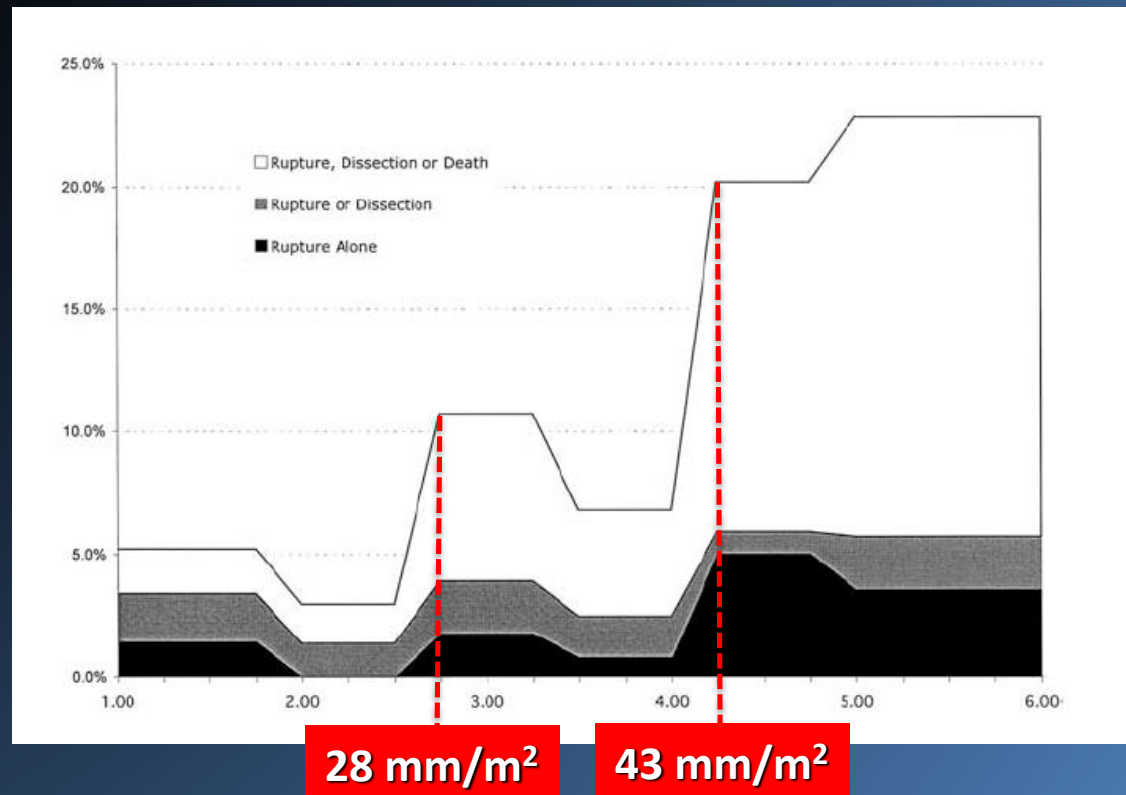


Relative aortic size predicts rupture or dissection of thoracic aortic aneurysms

Retrospective study: 410 patients with thoracic aortic aneurysms:
Aortic size index: maximal diameter indexed to BSA (mm/m^2)
= significant predictor of rupture, death, or dissection

Demographics at baseline:

- Age: 65 years (9-93)
- Male gender: N= 257 (63%)
- BSA: 1.9 m^2 (1.1-2.7)
- Hypertension: N= 356 (67%)
- Marfan : N= 23 (6%)



28 mm/m^2

43 mm/m^2



Relative aortic size predicts rupture or dissection of thoracic aortic aneurysms

Table 5. Risk of Complications by Aortic Diameter and Body Surface Area With Aortic Size Index Given Within Chart

	Aortic Size (cm)									
	3.5	4.0	4.5	5.0	5.5	6.0	6.5	7.0	7.5	8.0
BSA										
1.30	2.69	3.08	3.46	3.85	4.23	4.62	5.00	5.38	5.77	6.15
1.40	2.50	2.86	3.21	3.57	3.93	4.29	4.64	5.00	5.36	5.71
1.50	2.33	2.67	3.00	3.33	3.67	4.00	4.33	4.67	5.00	5.33
1.60	2.19	2.50	2.80	3.13	3.44	3.75	4.06	4.38	4.69	5.00
1.70	2.05	2.35	2.65	2.94	3.24	3.53	3.82	4.12	4.41	4.71
1.80	1.94	2.22	2.50	2.78	3.06	3.33	3.61	3.89	4.17	4.44
1.90	1.84	2.11	2.37	2.63	2.89	3.16	3.42	3.68	3.95	4.22
2.00	1.75	2.00	2.25	2.50	2.75	3.00	3.25	3.50	3.75	4.00
2.10	1.67	1.90	2.14	2.38	2.62	2.86	3.10	3.33	3.57	3.80
2.20	1.59	1.82	2.05	2.27	2.50	2.72	2.95	3.18	3.41	3.64
2.30	1.52	1.74	1.96	2.17	2.39	2.61	2.83	3.04	3.26	3.48
2.40	1.46	1.67	1.88	2.08	2.29	2.50	2.71	2.92	3.13	3.33
2.50	1.40	1.60	1.80	2.00	2.20	2.40	2.60	2.80	3.00	3.20

□ = low risk (~1% per yr); □ = moderate risk (~8% per yr); □ = severe risk (~20% per yr).

White area indicates low risk, light gray area indicates moderate risk, and dark gray area indicates severe risk.

BSA = body surface area.

NB: Non-Marfan (94%)



Aorta enlargement and bicuspid aortic valve associated with dissection in Turner Syndrome

- Data from 20 individuals with acute AD (Type A in 17 cases, 5%) from the International Turner Syndrome Aortic Dissection Registry

18 of 19 patients (95%) with AAD had an associated cardiac malformation that included a bicuspid aortic valve.

For those with type A dissections, the mean ascending aorta size index (ASI) was $2.7 \pm 0.6 \text{ cm/m}^2$

Patients with Turner syndrome aged >18 years with ASI >2.5 cm/m² should be considered for an aortic operation to prevent aortic dissection

Patient No.	Age at Dissection, y	Cardiac Diagnosis (Comment)	Hypertension (Y/N)	Location of Dissection	Symptom Duration	Outcome
	18	BAV	N	Type A	>24 hr	Death
	18	BAV, coarctation	Y	Type A	>24 hr	Death
	21	BAV	N	Type A	>24 hr	Alive
	23	BAV, h/o IAA	N	Type A	>24 hr	Death
	24	BAV, coarctation	N	Type A	>24 hr	Death
	27	BAV	N	Type A	>24 hr	Alive
	28	BAV	N	Type A	<24 hr	Alive
	28	BAV	Y	Type A	>24 hr	Death
	28	BAV, unrepaired coarctation	N	Type A	<24 hr	Death
	29	BAV	Y	Type A	>24 hr	Death
	29	BAV	N	Type B	<24 hr	Death
	30	BAV	Y	Type A	>24 hr	Death
	34	BAV	N	Type A	<24 hr	Death
	35	coarctation (dissection during stent)	Y	Type B	<24 hr	Alive
	37	BAV, VSD	Y	Type A	>24 hr	Death
	40	None	N	Type A	<24 hr	Death
	41	BAV	N	Type A	>24 hr	Alive
	44	BAV	N	Type A	>24 hr	Alive
	48	BAV/severe AS	Unknown	Type A	<24 hr	Alive
20*	48	BAV, aberrant RSA	Y	Type B	>24 hr	Alive
Mean, SD, med, 1st quart, 3rd quart (for type A dissections only)		30.5, 8.7, 28, 23.5, 38.5				

*Not previously reported, reference is given for known prior reports others may or may not have been reported.

AS indicates aortic stenosis; BAV, bicuspid aortic valve; IAA, interrupted aortic arch; VSD, ventricular septal defect; RSA, right subclavian artery.



Asymptomatic patients with Marfan Σ d: Aorta cross-sectional area to height ratio

Svensson et al. *J Thorac Cardiovasc Surg.* 2002;123: 361

Aortic Cross-sectional area / Height Ratio can be calculated as:

$$\text{Ratio} = \pi r^2 \text{ (cm}^2\text{)} / \text{height (m)}$$

Example of a 1,85 m male patient with a 5,0 cm aorta:

$$\text{Ratio} = 3,14 \times (5/2)^2 / 1,85 = \mathbf{10,6}$$

Example of a 1,65 m female patient with a 4,6 cm aorta:

$$\text{Ratio} = 3,14 \times (4,6/2)^2 / 1,65 = \mathbf{10,06}$$

**Marfan, Bicuspid AV: Prophylactic surgery advised in case of a
Ratio > 10 (ACC/AHA 2010; Class IIa)**



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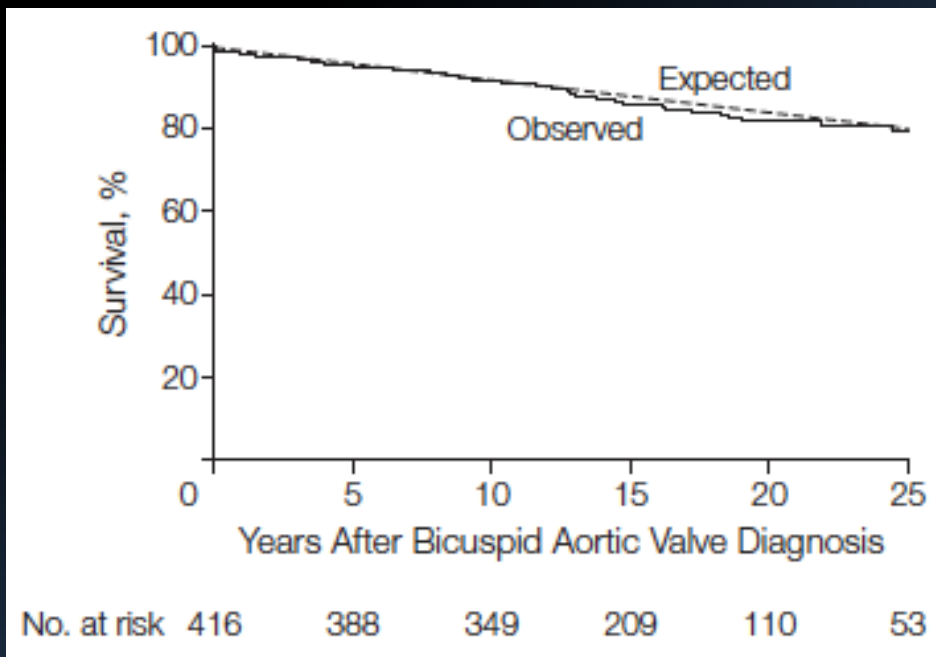
Thoracic aortic aneurysm

Apart from aorta size,
who is at highest risk?



Incidence of aortic complications in patients with bicuspid aortic valves

- Mean FU time of 16 ± 7 years / AORTIC DISSECTION occurred in 2 of 416 patients :
 - Incidence of 3.1 (95% CI, 0.5-9.5) cases per 10 000 patient-years,
 - Age-adjusted relative-risk 8.4 (95% CI, 2.1-33.5; $P=.003$) vs. general population.
- There were no dissections in patients with baseline aortic diameter <45 mm or with normally functioning aortic valves.



- Survival rate after 25 years was 80% (95% CI 74.2%-85.8%)
- It was identical to the expected survival of the general county population matched for age and sex ($P=0.98$)

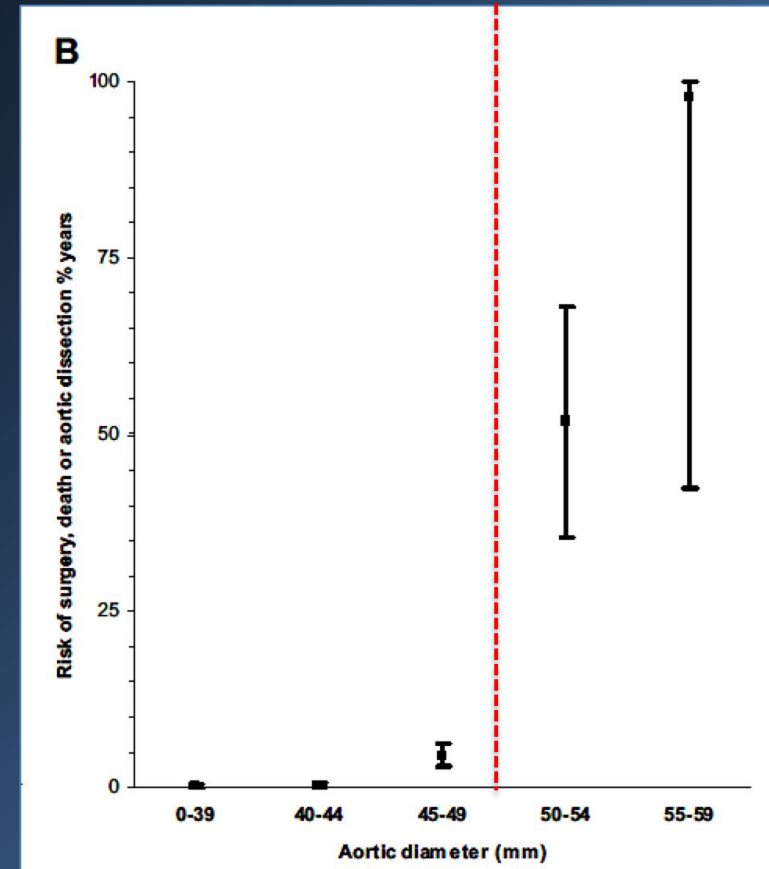


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Aortic events in the Marfan Population : A cohort study

- 732 patients with Marfan's Σ d, followed up for a mean of 6.6 years.
 - Systematic β -blockade/Advice about sports activities/Annual FU.
 - Prophylactic aortic surgery: maximal aortic diameter ≥ 50 mm.
 - Follow-up: 5 deaths and 2 dissections (Type A).
-
- The risk of death/ AAD increased 4 times at diameters ≥ 50 mm.
 - Aortic diameter < 50 mm: annual risk $< 0.05\%$ after exclusion of:
 1. A neonatal patient
 2. A woman who became pregnant against our recommendation
 3. A 72-year-old woman with previous myocardial infarction.

Jondeau et al. *Circulation*. 2012;125: 226-32





Non-syndromic thoracic aortic aneurysm: Outcomes vs. bicuspid AV and Marfan Σ

1988-2014: Prospective follow-up of all patients <60 years of age and genetic aortopathy:

1/ Bicuspid aortic valve (BAV), n=228

2/ Marfan syndrome (MFS), n=221

3/ Heritable TAA without obvious physical features = non-syndromic TAA (NS-TAA), n=311

TABLE 2 Clinical Features of Patients Enrolled in Clinical Surveillance

	NS-TAA (n = 253)	MFS (n = 209)	BAV (n = 225)	All Patients (N = 687)
Follow-up time, yrs	6.0 (2.0-12.0)	11.0 (6.0-18.0)*	7.0 (3.0-15.0)	7.0 (3.0-15.0)
Age, yrs	40.7 ± 12.3	27.8 ± 11.7*	38.8 ± 13.7	36.2 ± 13.7
Female	61 (24.1)	90 (43.1)*	39 (17.3)	190 (27.7)
Family history of aneurysm	154 (60.9)	136 (65.1)	35 (15.6)†	325 (47.3)
Family history of dissection	80 (31.6)	43 (20.6)*	5 (2.2)	128 (18.6)
Initial aortic diameter, mm‡	45.6 ± 10.5	41.9 ± 9.2§	44.1 ± 8.4	44.0 ± 9.5
Systolic BP, mm Hg	127.3 ± 15.5	117.6 ± 14.5*	128.0 ± 12.4	124.5 ± 15.0
Diastolic BP, mm Hg	77.4 ± 8.6	71.3 ± 9.0*	76.8 ± 8.7	75.3 ± 9.1

Values are median (interquartile range), mean ± SD, or n (%). *p < 0.001 versus NS-TAA and BAV. †p < 0.001 versus NS-TAA and MFS. ‡Available for n = 643 (93.6%). §p < 0.001 versus NS-TAA. ||p < 0.05 versus MFS.

Abbreviations as in Table 1.

The 687 patients surviving >30 days after presentation were followed for a median of 7 years.



Non-syndromic thoracic aortic aneurysm: Outcomes vs. bicuspid AV and Marfan Σ

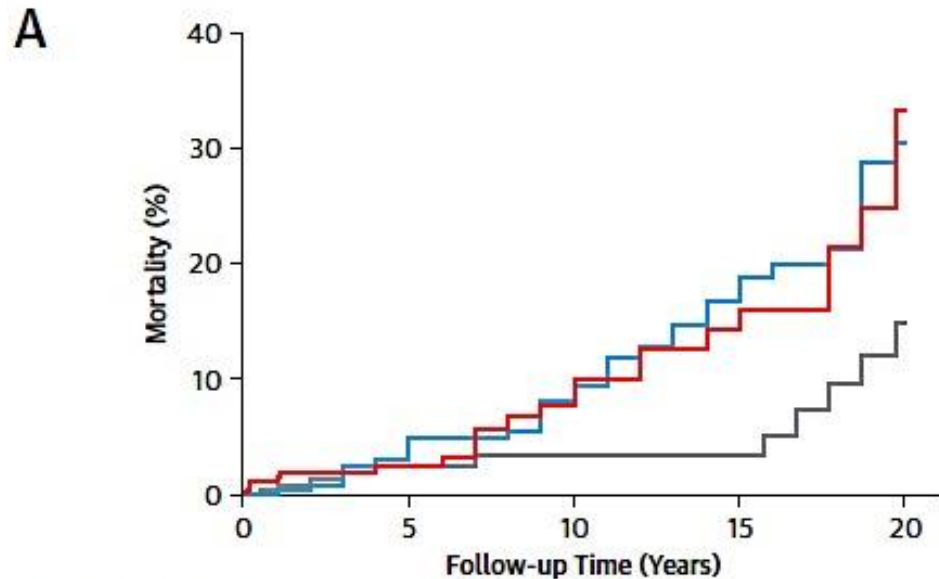
10-year mortality was 3.5% for BAV, 7.8% for NS-TAA and 8.7% for MFS: $p < 0.05$ for BAV vs. NS-TAA and MFS

Factors associated with all-cause mortality:

- Marfan syndrome ($p < 0.04$)
- Age at presentation
- Family history of dissection (doubling the mortality risk)

Aorta size = NS

FIGURE 1 Mortality in Clinical Surveillance Group



Number of patients at risk:

— NS-TAAD	253	149	81	49	17
— MFS	209	164	115	79	42
— BAV	225	140	91	60	31



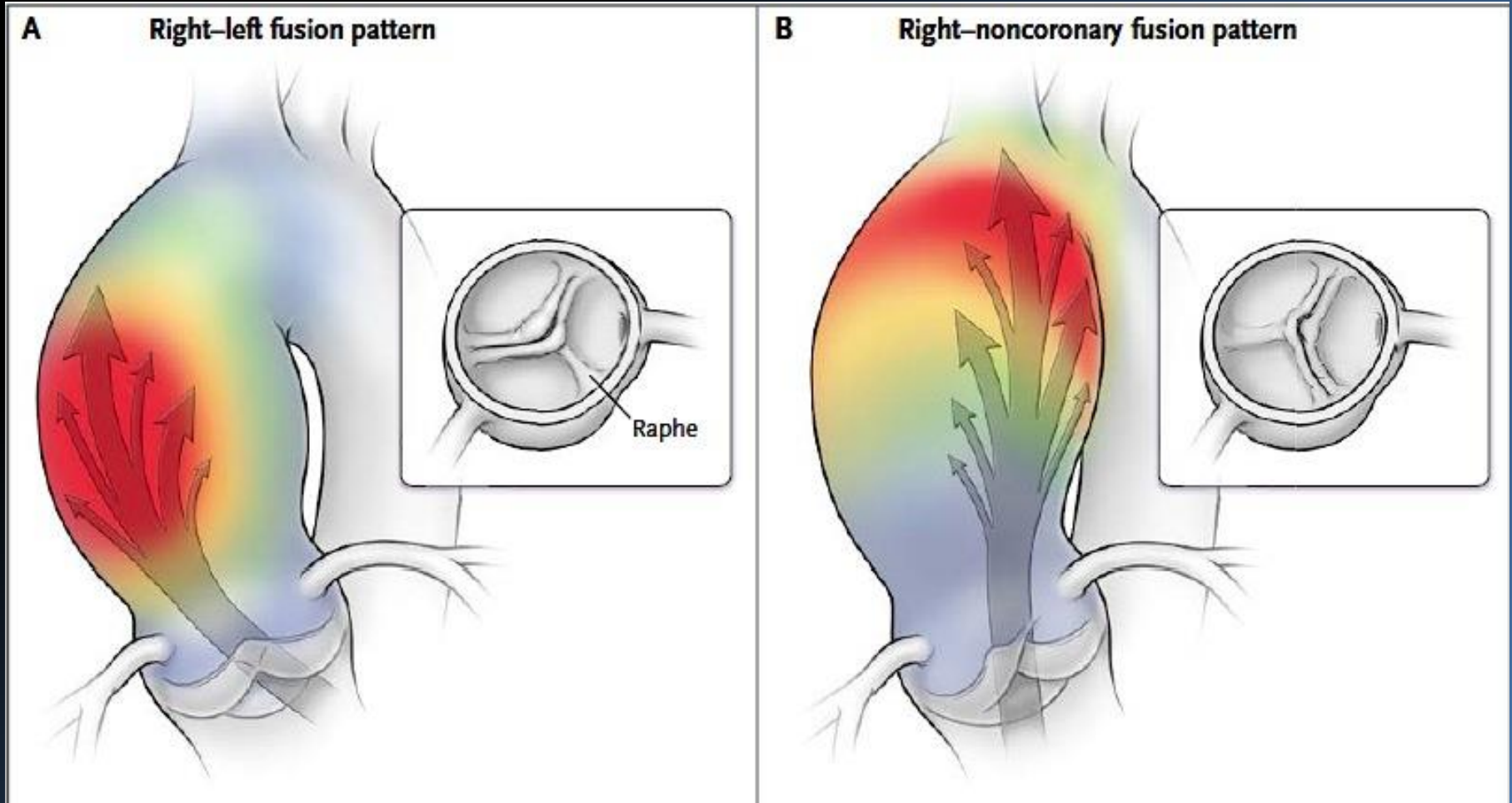
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Thoracic aortic aneurysm

Future directions:
Is there a role for MRI ?



Aortic dilatation in patients with bicuspid aortic valve

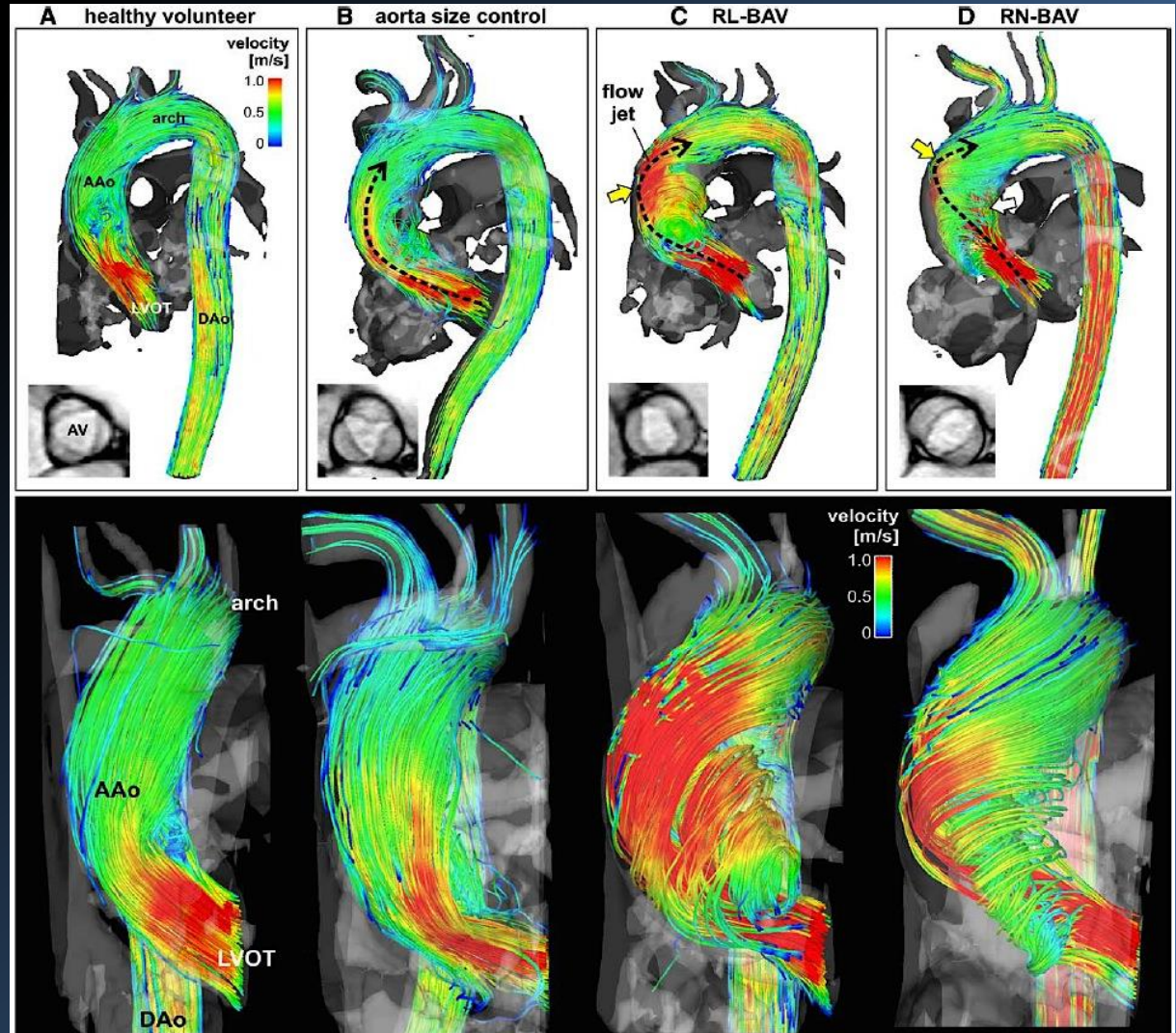




Bicuspid aortic cusp fusion alters aorta flow patterns (3D-MRI)

Four-dimensional flow-MRI can measure in vivo 3-D blood flow in the aorta

The type of BAV fusion is associated with regional wall shear stress distribution, systolic flow eccentricity and expression of BAV aortopathy





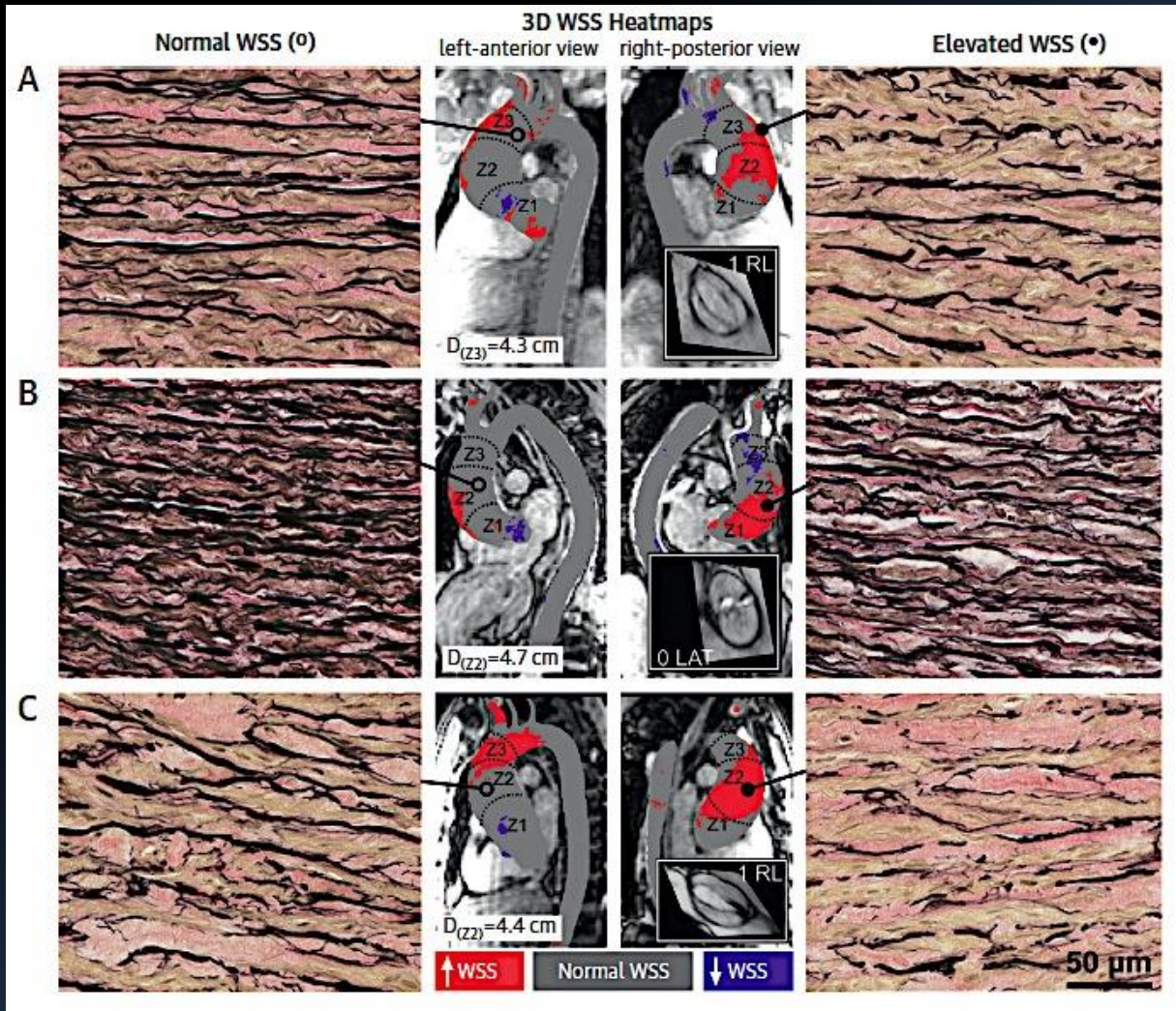
Valve-related hemodynamics mediate human bicuspid aortopathy

- BAV patients (n = 20) undergoing ascending aortic resection underwent pre-operative 4D-flow CMR to regionally map aortic **wall shear stress (WSS)**.
- Paired aortic wall samples (within-patient samples obtained from regions of elevated vs. normal WSS) were collected and compared for medial elastin degeneration by histology and **extra-cellular matrix (ECM)** regulation by protein expression (mainly MMP and TGF β).

TABLE 1 Patient Characteristics in BAV Study Population (N = 20)

Age, yrs	48 \pm 15
Female	2 (10)
BAV classification	
Type 0, lateral	2 (10)
Type 1, RN	1 (5)
Type 1, RL	12 (60)
Type 2, RL/RN	5 (25)
Aortic diameter, cm	
Sinus of Valsalva	4.4 \pm 0.5 (range 3.7-5.7)
Mid ascending aorta	4.7 \pm 0.6 (range 3.6-6.3)
Aortic valve function	
No AS, moderate/severe AR	5 (25)
Mild AS, moderate/severe AR	1 (5)
Moderate/severe AS, no AR	5 (25)
Moderate/severe AS, mild AR	3 (15)
Moderate/severe AS, moderate/severe AR	6 (30)
Hypertension	7 (35)
Surgical procedure: aortic valve	
Repair	1 (5)
Replacement	19 (95)
AVR	4 (20)
Bentall	14 (70)
Ross	1 (5)
Surgical procedure: AsAo	
AsAo replacement	20 (100)
Root replacement	16 (80)
Hemi-arch	8 (40)

Valve-related hemodynamics mediate human bicuspid aortopathy



Regions of high wall shear stress (WSS) had:

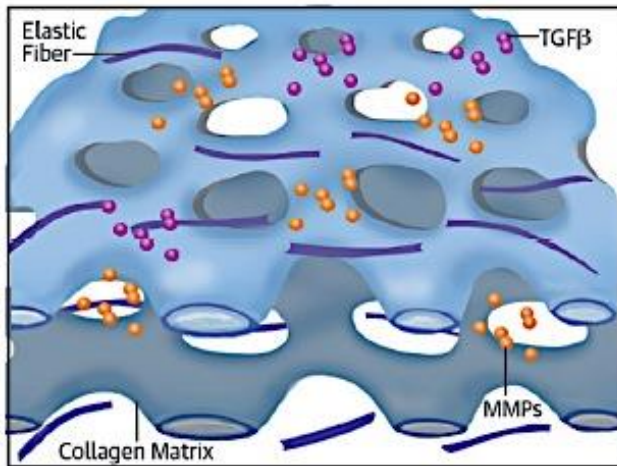
1. Fewer elastin fibers (black)
2. Thinner Elastin fibers
3. farther apart

as compared with regions with normal WSS

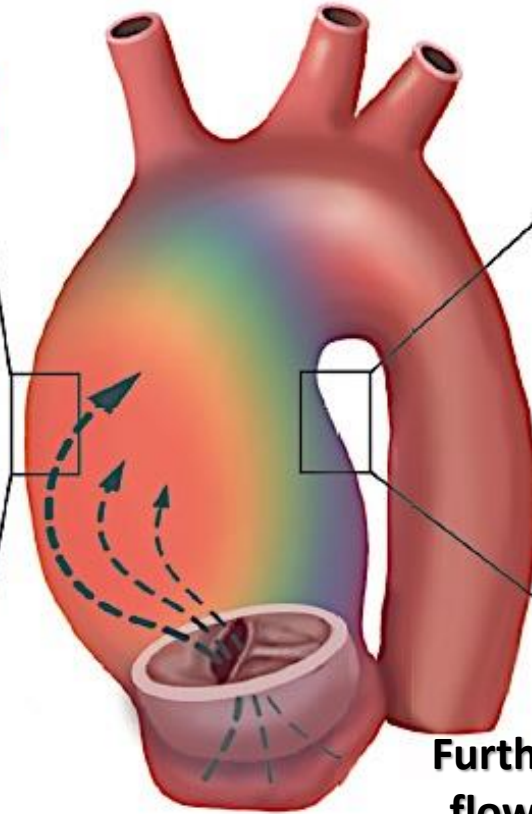
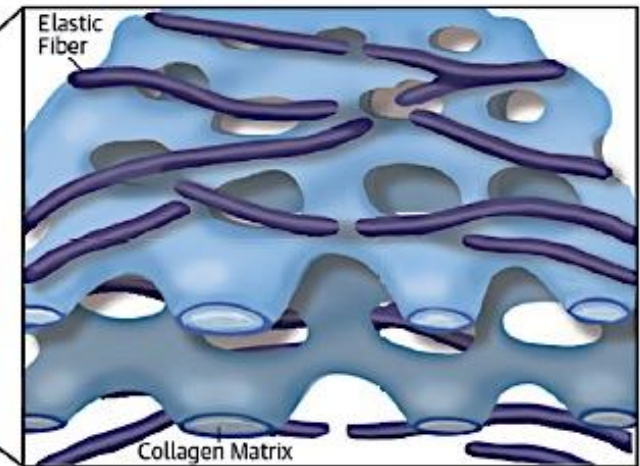


Valve-related hemodynamics mediate human bicuspid aortopathy

Elevated WSS



Normal WSS



Further study to validate the use of 4D flow CMR as a noninvasive biomarker of disease progression and its ability to individualize resection strategies is warranted



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Thoracic aortic aneurysm

What do the Guidelines tell us?



Indications for intervention on aneurysms of the ascending aorta

RECOMMENDATIONS	Class	LOE
Surgery is indicated in patients with Marfan's syndrome and aortic root aneurysm with maximal aortic diameter >50 mm.	I	C
Surgery should be considered in patients with aortic root aneurysm, and maximal ascending aortic diameters: <ul style="list-style-type: none">• > 45 mm for patients with Marfan's syndrome AND risk factors• > 50 mm for patients with a bicuspid valve AND risk factors• > 55 mm for other patients with no elastopathy	IIa	C
Lower thresholds for intervention may be considered in patients of <u>small stature</u> * or in case of rapid progression, aortic valve regurgitation, planned pregnancy and patient's preference.	IIb	C

* in patients with Turner syndrome, an indexed aortic diameter of 27.5 mm/m² should be considered

Indications for surgery in aortic root disease (whatever the severity of AR)

	Class	Level
Surgery is indicated in patients who have aortic root disease with maximal ascending aortic diameter ≥ 50 mm for patients with Marfan syndrome	I	C
Surgery should be considered in patients who have aortic root disease with maximal ascending aortic diameter: <ul style="list-style-type: none">• ≥ 45 mm for patients with Marfan syndrome with risk factors,• ≥ 50 mm for patients with bicuspid valve with risk factors,• ≥ 55 mm for other patients.	Ila	C

RISK FACTORS:

Marfan + BAV: **Family history of dissection**, Increase in aortic diameter >2 (5) mm/year

Marfan: Severe AR/ MR, Desire of pregnancy

BAV: Coarctation of the aorta, Systemic hypertension



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Bicuspid aortic valves: Indications for surgery

Class IIa : Replacement of the ascending aorta is reasonable in patients with a bicuspid aortic valve who are undergoing aortic valve surgery because of severe AS or AR if the diameter of the ascending aorta is greater than 4.5 cm. (Level of Evidence: C)

Replacement of the sinuses of Valsalva is not necessary in all cases and should be individualized based on the displacement of the coronary ostia, because progressive dilation of the sinus segment after separate valve and graft repair is uncommon.



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Thoracic aortic aneurysm

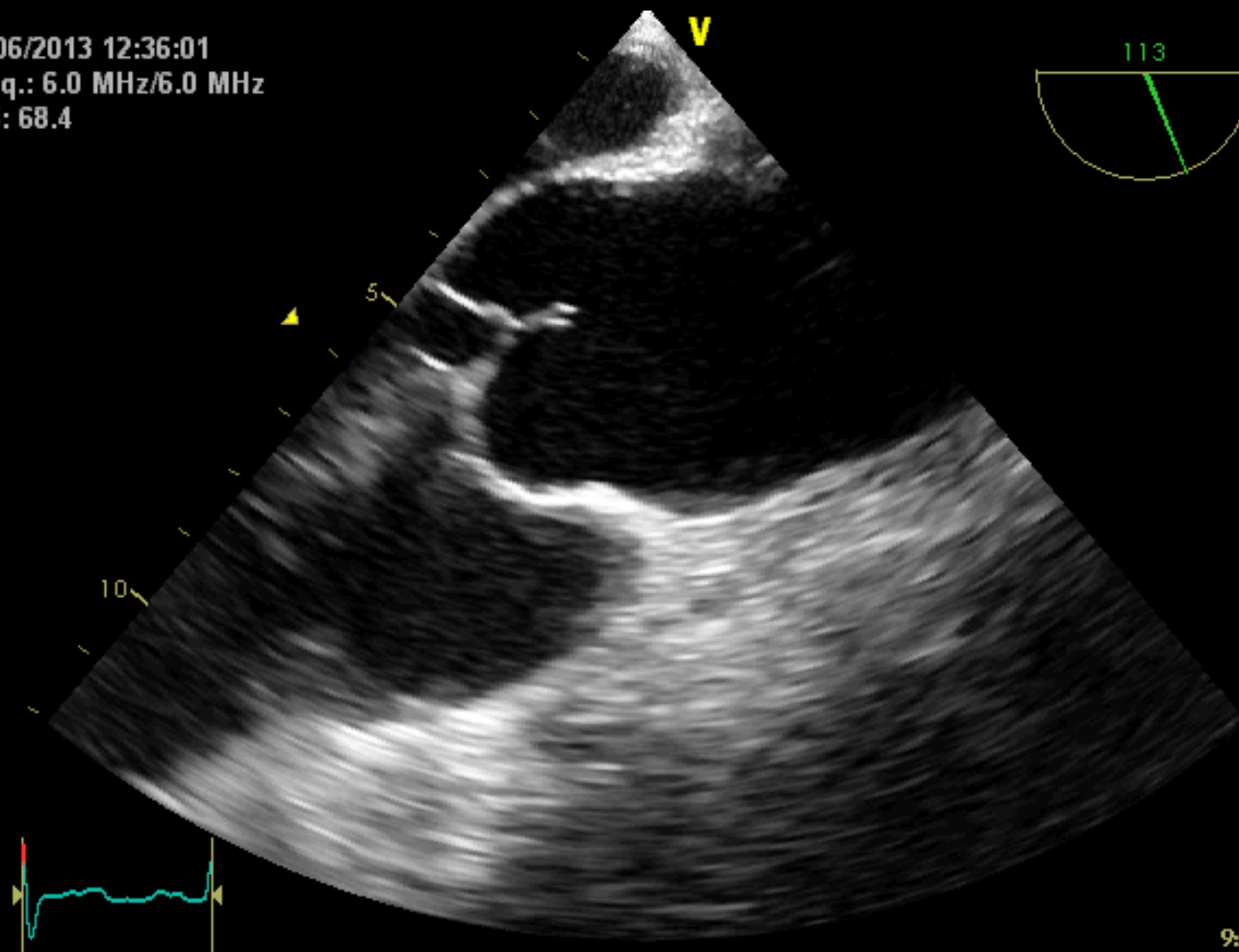
What about our patient?
Unexplained sudden death in her
younger sister:
strong suspicion of genetic
(non-syndromic) aneurysm



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Transesophageal Echo:

17/06/2013 12:36:01
Freq.: 6.0 MHz/6.0 MHz
IPS: 68.4



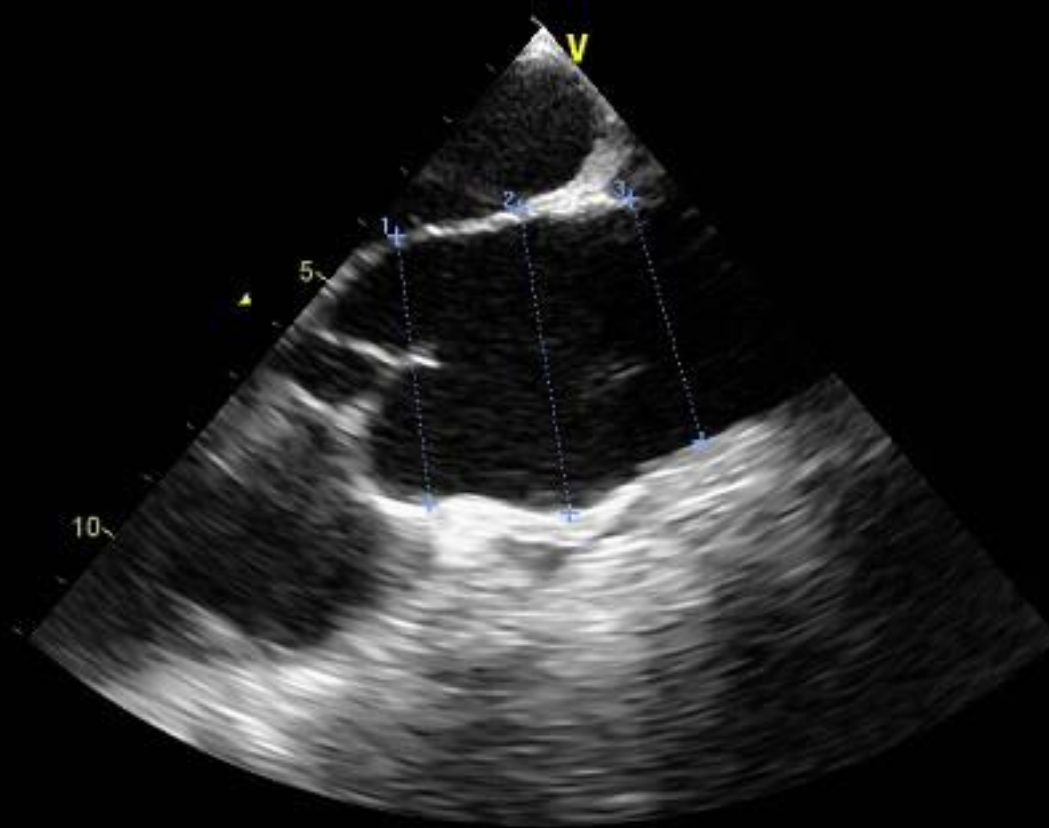
94
9:60 HR



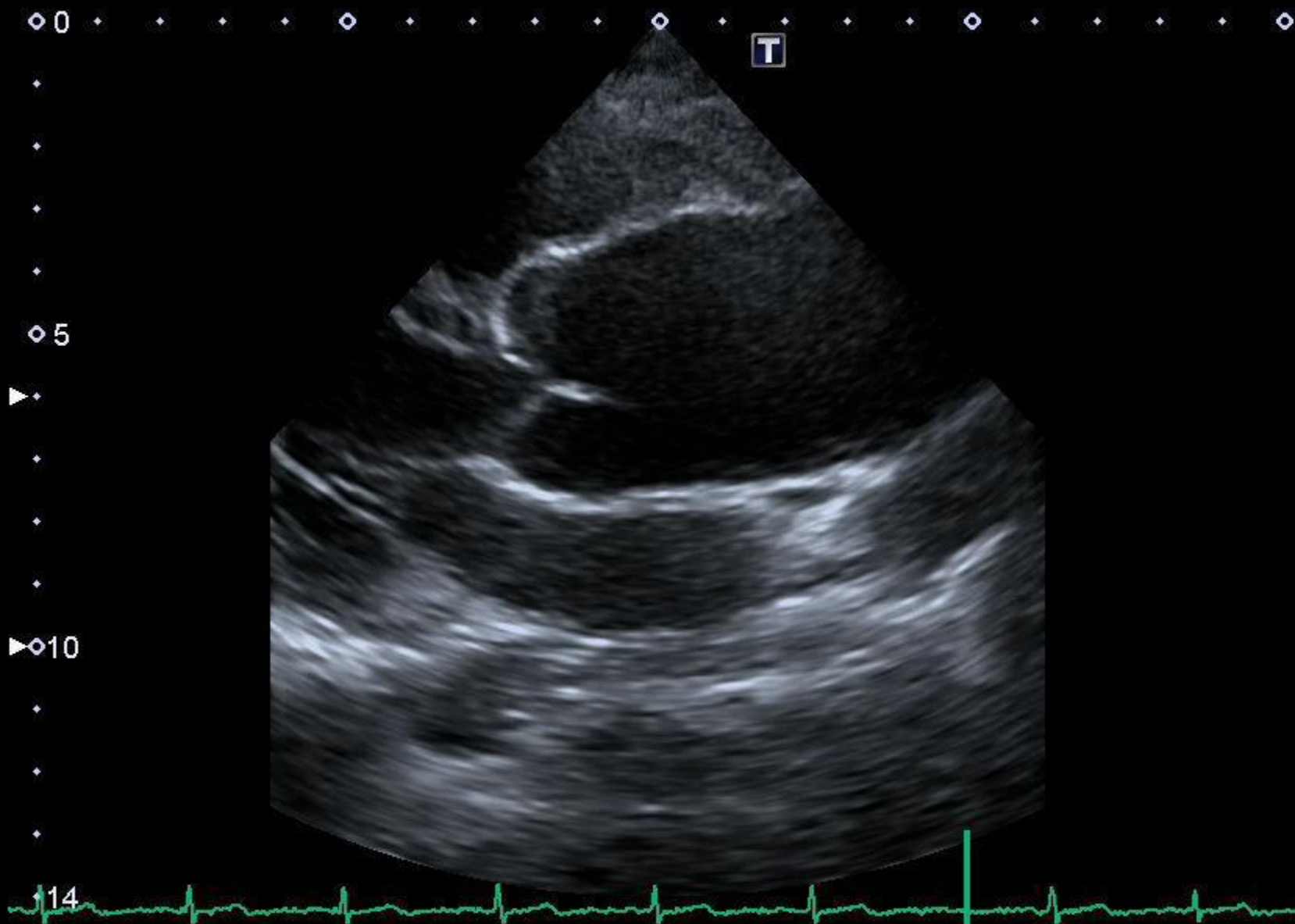
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Transesophageal Echo:

● 164°
3 L 3.78 cm
2 L 4.60 cm
1 L 4.03 cm



92
HR



M
1.4
5S2
T2.4
46 fps
Qscan
G:86
DR:70



Cardiac CT scan

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Oblique
Ex: 10061
Se:2
L: 29.94 (col)
DFOV 16.3cm

A
1
0
4

Average
2.21

0.6mm 0.22:1 / 0.62sp

08:30:59 AM
W = 749 L = 158

SR

4913015205
41
F
DoB: Jun 18 1972
Ex: Jun 19 2013

P
-5
-9
S

Average
2.21

0.6mm 0.22:1 / 0.62sp

08:30:59 AM
W = 624 L = 326

Volume 2
Oblique
Ex: 10061
Se:104
L: 109.09 (col)
DFOV 16.3cm

SRA

4913015205
41
F
DoB: Jun 18 1972
Ex: Jun 19 2013

P
-5
-9
S

Average
2.21

0.6mm 0.22:1 / 0.62sp

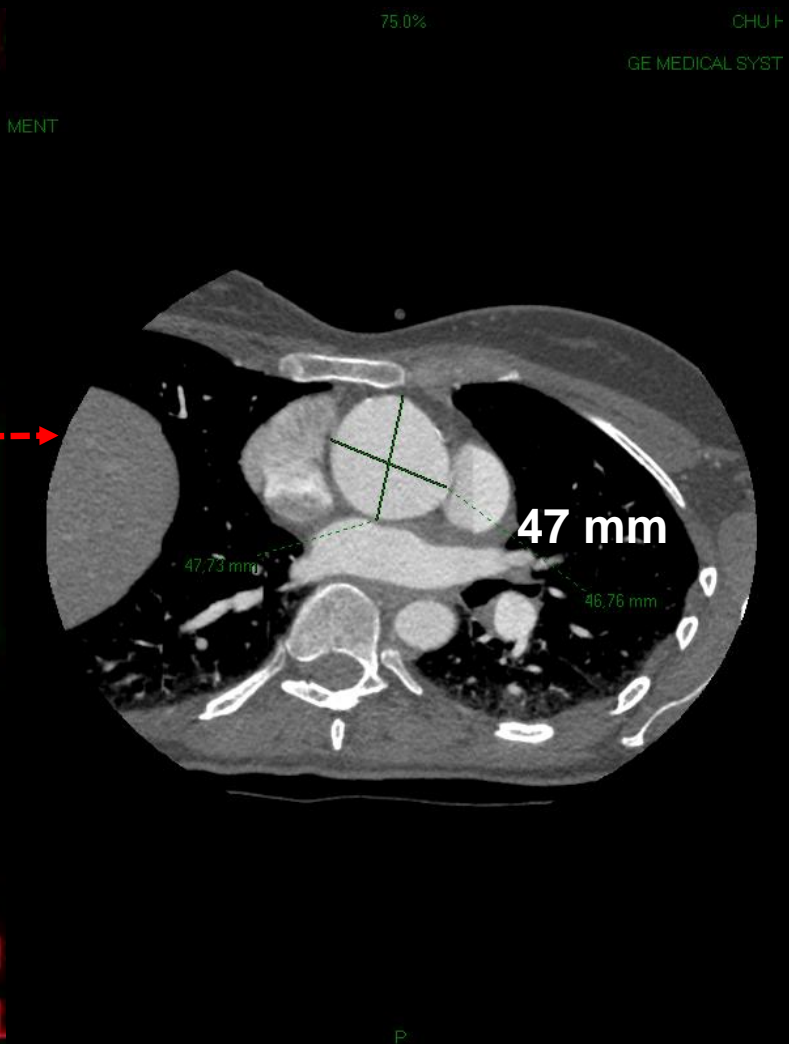
08:30:59 AM
W = 624 L = 326

IUP



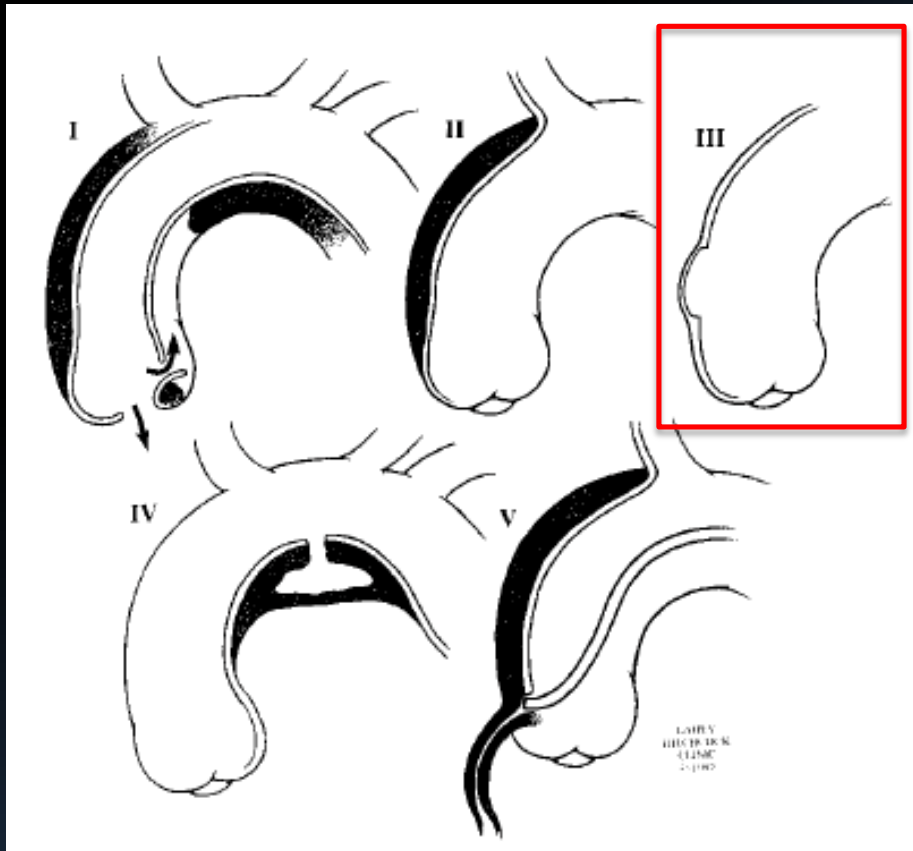
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Cardiac CT scan



Intimal tear without hematoma:

An Important Variant of Aortic Dissection That Can Elude Current Imaging Techniques



- **Class 1:** Classic aortic dissection: flap between true/ false lumen
- **Class 2:** Intramural hematoma
- **Class 3:** Limited intimal tear: eccentric bulge at tear site
- **Class 4:** Penetrating atherosclerotic ulcer
- **Class 5:** Iatrogenic/ traumatic dissection



Clinical case: conclusion

She underwent surgery with confirmation of localized intimal tear and impending rupture.

Uneventful postoperative course and she became pregnant 6 months thereafter



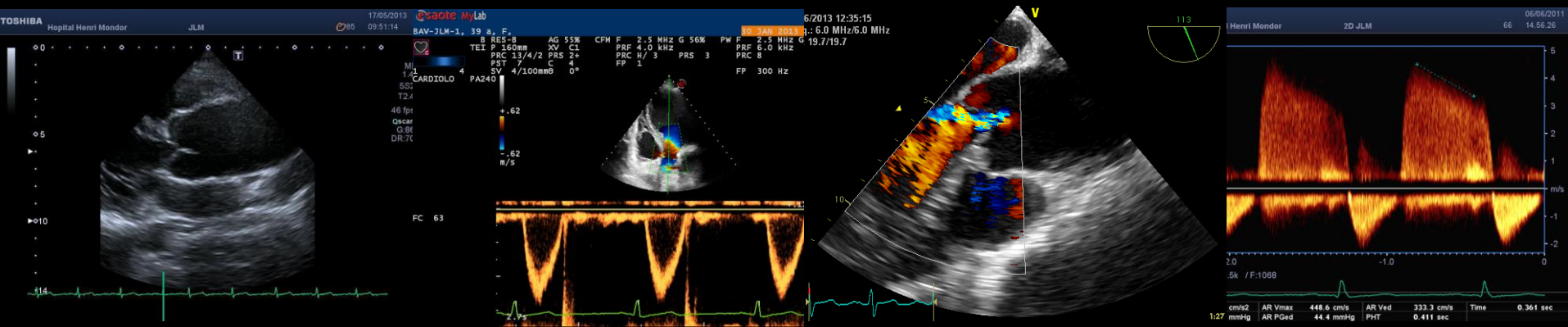
Take-Home Messages

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- **Current Guidelines:** prophylactic surgery for proximal aortic aneurysm >55 mm to prevent acute aortic dissection or rupture
- Indexed cutoff values are currently not clear
- **Additional risk factors are crucial for considering earlier surgery:**
 - For any patient: Family history of AAD/ aortic rupture,
Rapid aorta growth (≥ 4 -5 mm/ year)
 - Bicuspid AV: Hypertension, coarctation (EU)
 - Marfan syndrome: surgery if aortic root >50 mm;
 >45 mm if desire of pregnancy, significant AR or MR; **consider surgery if aorta cross-sectional area/height ratio >10**
 - Turner syndrome: surgery if proximal aorta > 25 mm/m²



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Management of pregnant women with bicuspid aortopathy

Before pregnancy

- Women with a bicuspid aortic valve should undergo imaging of the entire aorta before pregnancy
- **Women with proximal aorta dimension >45 mm should be advised against pregnancy**
- Women with mildly dilated proximal aorta (40-45 mm) likely represent an intermediate risk group for which pregnancy is relatively contraindicated and who will require close medical surveillance during pregnancy



Management of pregnant women with bicuspid aortopathy

Before pregnancy (2)

- **Threshold for surgery prior to pregnancy is similar to that of the general population of individuals with bicuspid aortopathy without concomitant valve dysfunction (50-55 mm)**
- **Body surface area should be taken into account in small women.**
- **Indexed aortic diameter has been proposed for pre-pregnancy surgical consideration but the suggested threshold was extrapolated from women with Turner's syndrome (*i.e.* 25-27 mm/m²)**



Management of pregnant women with bicuspid aortopathy

Antepartum and Peripartum

- Women with a dilated aorta should have strict blood pressure control
- Repeated echocardiographic imaging every 4–12 weeks during pregnancy should be performed in women with bicuspid aortopathy
- MRI (without gadolinium) is recommended if there is an indication for imaging of distal ascending aorta, aortic arch or descending aorta during pregnancy



Management of pregnant women with bicuspid aortopathy

Antepartum and Peripartum (2)

- Beta adrenergic blockers, to reduce shear stress on the aorta, may be considered during pregnancy in women with dilated aorta
- Women with bicuspid aortopathy or history of dissection should deliver in a centre where cardiothoracic surgery is available
- **Cesarean delivery should be considered for aorta > 45 mm**
- For women with aorta < 40 mm, Cesarean delivery is reserved for obstetric or fetal indications